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Successful Scale-up via Simulation of Production Vessels under Lab Conditions

Ray Machado, David Ford, Dom Hebrault†
Reaction Engineering
Mettler-Toledo Autochem
7075 Samuel Morse Drive
Columbia, MD 21046

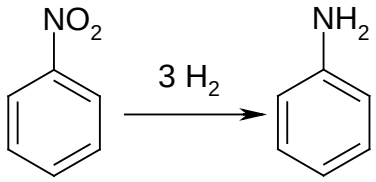
† Presenter e-mail: dominique.hebrault@mt.com

Abstract

Understanding and minimizing the thermal risks of chemical processes is a critical part of sustainable process development and scale-up. Sophisticated and dedicated analytical instrumentation, for instance reaction calorimetry with RC1e, has been used to determine reaction kinetics and thermodynamics[1]. Now, even simpler and more affordable technologies with higher throughput provide chemists and engineers with the required thermodynamic data-rich experiments early-on for state-of-the-art process development. In this example, we discover how 1- The reduction of a nitroaromatic, 2- The production of a heteroatom-rich heterocycle, have been made safer, and more efficient through the use of a combination of reaction calorimetry, computer controlled experiments, and process analytical technologies. In each example, these technologies provided a better kinetic and mechanistic understanding, resulting in enhanced batch or continous (CSTR or plug flow) processes.

Reduction of a nitroaromatic compound

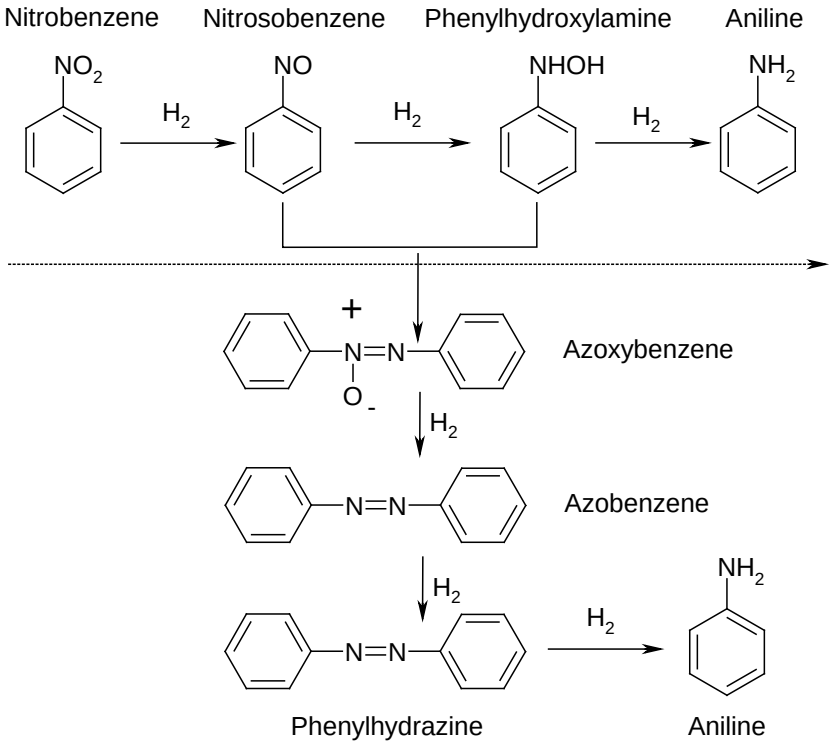
The hydrogenation of nitro compounds is highly exothermic, and as such, their safety profile and heat of reaction must be carefully investigated before any scale-up is attempted[2]. An appropriate first step is to explore the various mechanistic pathways hidding behind the simplicity of the hydrogenation equation.
Although the reduction of nitroaromatic compounds can be written as per equation 1, experimental evidence shows a more complex mechanistic pathway.



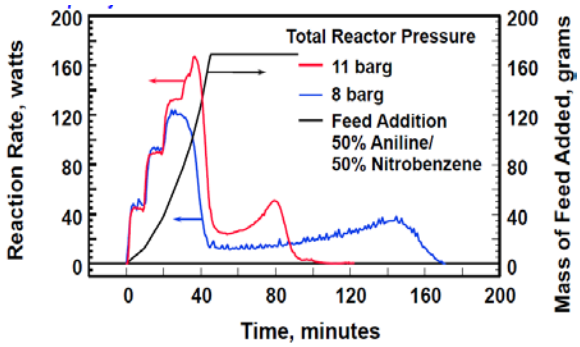
$\Delta H_{reaction}$ = - 537 kJ / mol

Equation 1

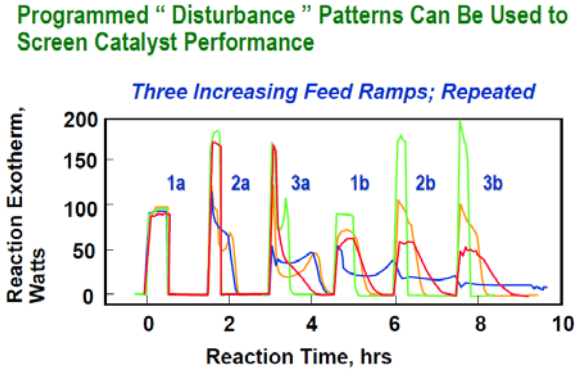
For instance, increasing hydrogen pressure, or temperature, increases the reaction rate, to some extent, as expected from the reaction depicted by equation 1. However, passed a certain point, the reaction rate, or heat rate, decreases sharply. Indeed, a more complex mechanistic pathway is generally admitted, as in equation 2.[3] It shows that instead of a direct conversion of nitrobenzene into aniline, nitrosobenzene, and phenylhydroxylamine are formed as intermediates, and can be isolated (path 1). They both can also react with each other to yield azoxybenzene, azobenzene, phenylhydrazine, itself hydrogenated into aniline (path 2 to aniline). This relatively complex reaction mechanism to aniline (path 1 and 2) was thoroughly investigated using reaction heat and HPLC for monitoring. A combination of computer-controlled experiments and lab scale process automation (RC1e calorimetry) was used to screen process variables, such as temperature, pressure, feed rate, and nature of the catalyst (graph 1 and 2).



Equation 2



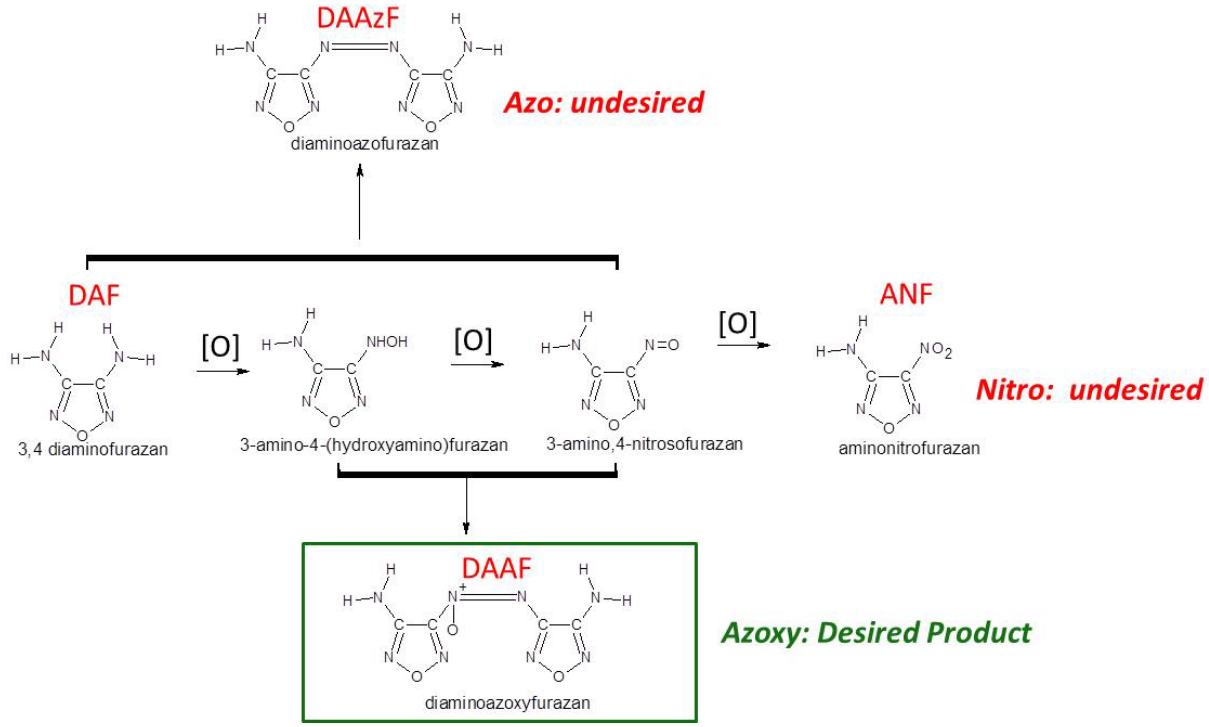
Graph 1



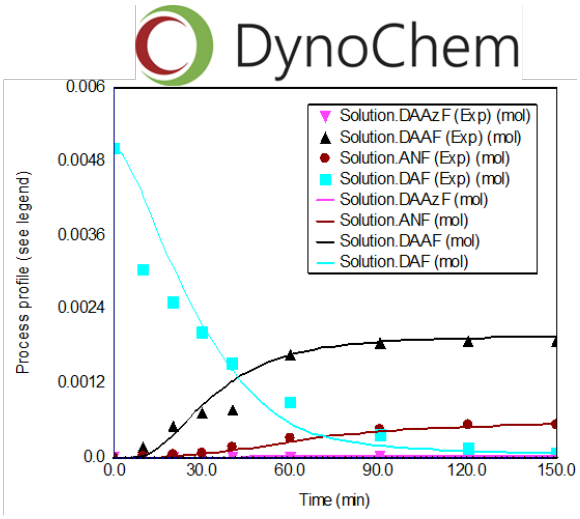
Graph 2

Dimerization of an amine to an azoxy compound

Nitrogen-rich heterocycles are well known for their reactivity and their sensitivity to shocks, which makes many of them suitable as explosives[4]. En route to diaminoazoxyfurazan (DAAF) from 3,4-diaminofurazan (DAF), as shown in equation 3, we embarked on an extensive scale-up study which target was to produce kilogram quantity of DAAF using continuous processing. Continous processing was deemed a safer alternative to batch processing considering the highly reactive nature of most reaction components. Through kinetic modeling and in-depth analytical examination, various side-products and intermediates were identified. DAF oxidizes into 3-amino-4-(hydroxyamino)furazan, and 3-amino-4-nitrosofurazan. Both react together to yield the targeted compound DAAF. Over-oxydation of 3-amino-4-nitrosofurazan produces aminonitrofurazan (ANF). Also, DAF and 3-amino-4-nitrosofurazan react to produce the undesired diaminoazofurazan DAAzF (equation 3). A kinetic model including all identified components, intermediates and side-products, was generated using the DynoChem software[5] (graph 3).

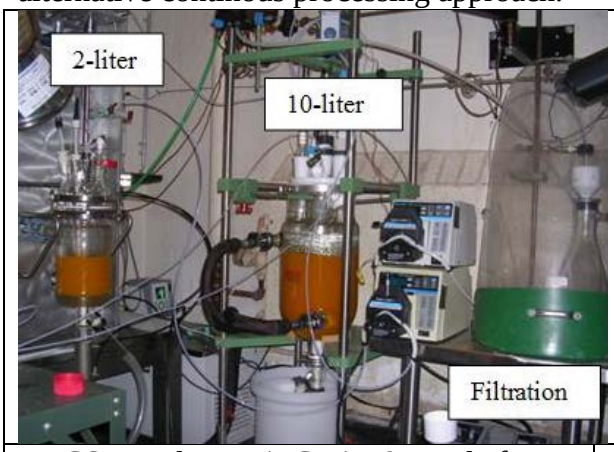


Equation 3



Graph 3

The kinetic model allowed to use the Levenspiel plot method[6] to dimension the continuous processing equipment suited to produce 200g/h of DAAF. Both the CSTR and plug flow reactor approaches were investigated and used for production (picture 1 and 2). A CSTR combination of 2L (RC1e), 10L (pilot scale), and 50L reactors (manufacturing scale) were used to produce kilogram scale quantity of DAAF. A Corning Advanced-Flow™ Reactor was used as an alternative continous processing approach.



CSTR pilot 2L (RC1e)-10L scale for DAAF production

CSTR manufacturing 50L scale for DAAF production

References

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(4) M. Riad Manaa*, Evan J. Reed, Laurence E. Fried and Nir Goldman; *J. Am. Chem. Soc.*, **2009**, *131* (15), pp 5483– 5487
(5) https://www.scale-up.com/
(6) http://ocw.mit.edu/courses/chemical-engineering/10-37-chemical-and-biological-reaction-engineering-spring-2007/lecture-notes/lec09_03072007_w.pdf